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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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10/587,678

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EXAMINER

ORWIG, KEVIN S

ART UNIT

PAPER NUMBER

1611

MAIL DATE

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PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No. 10/587,678	Applicant(s) UHRICH ET AL.	
	Examiner Kevin S. Orwig	Art Unit 1611	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on Nov. 10, 2008.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1,2,8-23,88,240 and 241 is/are pending in the application.
- 4a) Of the above claim(s) 88 is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 1,2 and 8-23, 240, and 241 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
- ☐ Certified copies of the priority documents have been received.
 - ☐ Certified copies of the priority documents have been received in Application No. _____.
 - ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- | | |
|--|---|
| 1) <input checked="" type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413) |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | Paper No(s)/Mail Date. _____ |
| 3) <input checked="" type="checkbox"/> Information Disclosure Statement(s) (PTO/SB/08) | 5) <input type="checkbox"/> Notice of Informal Patent Application |
| Paper No(s)/Mail Date <u>11/17/06</u> . | 6) <input type="checkbox"/> Other: _____ |

DETAILED ACTION

Status of the Claims

Claims 1, 2, 8-23, 88, 240, and 241 are currently pending. Claims 1, 2, 8-23, 240 and 241 are the subject of this Office Action. This is the first Office Action on the merits of the claims. Non-elected claim 88 is withdrawn from consideration.

Election/Restrictions

Applicants' election of Group III (claims 2, 8-23, 240 and 241, as stated by applicant) in the reply filed on Nov. 10, 2008 is acknowledged. In response to applicants' election, Group II (claim 88) is withdrawn from further consideration pursuant to 37 CFR 1.142(b) as being drawn to a nonelected invention, there being no allowable generic or linking claim. It is noted that the claims encompassed within each group were modified per applicants' amendments in the reply. Additionally, upon further consideration, the examiner hereby WITHDRAWS the election requirement between Groups I and III due to the similarity of the subject matter as currently claimed. Thus claim 1, drawn to a method of sequestering LDL, will be examined along with Group III. Applicants have elected Group III with traverse.

The traversal is on the ground(s) that the compounds recited in the instant application are non-overlapping with those disclosed in WO 03/005959 (cited to break unity). While this appears to be the case, as clarified by applicants' species election in the reply, the compounds in WO 03/005959 are essentially polymeric forms of the instantly claimed compounds, and thus share significant structural similarity.

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Furthermore, the instantly claimed method is an obvious use of the claimed compounds, which were known in the art at the time of the invention as discussed below. As, such the instantly claimed method cannot be considered a contribution over the prior art and the claims are subject to restriction. As stated above, the requirement for restriction between groups I and III is hereby WITHDRAWN, however the requirement for restriction between Group II and the other Groups is MAINTAINED. The restriction requirement is still deemed proper and is therefore made FINAL.

Claim 88 is withdrawn from further consideration pursuant to 37 CFR 1.142(b), as being drawn to a nonelected invention, there being no allowable generic or linking claim. Claims 1, 2, 8-23, 240, and 241 are under consideration to the extent of applicants' elected species.

Information Disclosure Statement

The references provided on the information disclosure statement(s) were considered and have been made of record.

Claim Rejections - 35 USC § 112 (2nd Paragraph)

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

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Claim 23 is rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 23 recites the limitation "the compound of chemical formula (I) or (II)" in line 2 of the claim. There is insufficient antecedent basis for this limitation in the claim as formula II is not recited in claim 240.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

The factual inquiries set forth in *Graham v. John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation

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under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 1, 2, 8-23, 240 and 241 are rejected under 35 U.S.C. 103(a) as being unpatentable over TIAN (Tian *et al.* Polymer Preprints (2002) 43(2); 719-720) in view of UHRICH (WO 03/005959; Published Jan. 23, 2003; 2nd reference on IDS dated Nov. 17, 2006) (hereinafter '959).

1. Tian discloses amphiphilic molecules of the structure depicted in formula III of instant claim 22 (elected species) that form stable polymeric micelles (page 719, left column, 2nd paragraph; Scheme 1; 1st paragraph of Results and Discussion section). Tian teaches that these molecules are intermediates in the preparation of amphiphilic star-like macromolecules (ASMs) (2nd paragraph of Introduction). Tian teaches that these micelles have hydrophobic cores suitable as “microcontainers” for lipophilic compounds and that the hydrophilic/lipophilic ratios (HLB) can be controlled by changing the length of the PEG or acyl chains (first paragraphs of Introduction and Results and Discussion sections). Tian teaches that the micelles form 20 nm diameter aggregations (i.e. nanoparticulates).

2. While Tian discloses the molecules of applicants' elected species, and suggests that they have utility for the encapsulation of hydrophilic compounds, Tian does not explicitly teach the use of these compounds to remove low-density lipoproteins (LDL) or to treat atherosclerosis. Since Tian does not specifically disclose what types of

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molecules may be encapsulated within the micelles, one would be motivated to look to the related literature for guidance regarding such usage.

3. Uhrich discloses polymeric compounds that form stable micelles in solution, wherein the micelles have a hydrophobic core and act as microcontainers for lipophilic compounds (abstract; 1st paragraph on page 2). Like the molecules of Tian, the hydrophobicity of Uhrich's compounds can be controlled by changing the length of the PEG or acyl chains (2nd paragraph on page 34). Uhrich teaches that these micelles are particularly useful for solubilizing hydrophobic molecules (page 26, 1st paragraph; and page 34, last paragraph). Uhrich teaches the use of these compounds to sequester lipoproteins such as LDL that contribute to atherosclerosis (page 10, 4th paragraph, elements (a) and (c)) by administering them to a patient in need of reducing the concentration of lipoproteins (page 10, end of 4th paragraph). Uhrich teaches that such administration can minimize cardiovascular diseases, such as atherosclerosis, caused by the presence of excess LDL in the blood (page 10, end of 4th paragraph).

4. Uhrich discloses embodiments of the compounds wherein they may contain the molecules taught by Tian (i.e. the instantly claimed molecules) as a part of their structure. For example, see Scheme 2 (top of page 26) discloses non-PEGylated versions of the instantly claimed molecules. It is noted that Uhrich teaches the use of polyethylene glycol (i.e. PEGylation) with these molecules (page 29, 2nd paragraph). Additionally, Figure 10 teaches an embodiment wherein four of Tian's molecules are incorporated into a polyol core, the only difference being that the embodiment depicted in the figure contains an amide instead of an ester linkage between the mucic acid

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moiety and the mPEG moiety. It is noted that replacement of this amide by an ester is taught in Uhrich's disclosure (see description of the compounds on pages 2-8, particularly embodiment d) on page 7, and the description of R⁴ in this embodiment on page 8). Thus, consistent with Tian's teaching, Tian's molecules are intermediates in the ASMs of Uhrich.

5. Given the similarity of the micelles formed by each of these molecules, and their identical intended uses to encapsulate hydrophobic compounds, it would have been *prima facie* obvious to one of ordinary skill in the art at the time of the invention to utilize the molecules of Tian to treat atherosclerosis by sequestering or removing LDL as taught by Uhrich. One would have been motivated to do so since Tian suggests that the molecules are suitable for use with hydrophobic compounds, but does not teach which specific compounds are suitable. Thus, the ordinary artisan would have readily envisioned the use of Tian's intermediates in the same manner as the macromolecular ASMs of Uhrich. Further, the artisan would be motivated to use Tian's molecules since they are simpler than those of Uhrich and therefore would be easier and cheaper to prepare. The similarity of the micelles and use of both Tian's intermediates and Uhrich's ASMs would have provided the artisan with a high expectation that Tian's molecules would function in a substantially similar way and be useful in the treatment of atherosclerosis by sequestering LDL in the hydrophobic core.

Thus, claims 1, 2, 8-23, 240, and 241 are obvious over Tian and Uhrich.

A reference is good not only for what it teaches by direct anticipation but also for what one of ordinary skill in the art might reasonably infer from the teachings. (*In re*

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Opprecht 12 USPQ 2d 1235, 1236 (Fed Cir. 1989); *In re Bode* 193 USPQ 12 (CCPA) 1976). In light of the forgoing discussion, the examiner concludes that the subject matter defined by the instant claims would have been obvious within the meaning of 35 USC 103(a). From the teachings of the references, it is apparent that one of ordinary skill in the art would have had a reasonable expectation of success in producing the claimed invention. Therefore, in the absence of evidence to the contrary, the invention as a whole was *prima facie* obvious to one of ordinary skill in the art at the time the invention was made, as evidenced by the references.

Conclusion

No claims are currently allowable.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Kevin S. Orwig whose telephone number is (571)270-5869. The examiner can normally be reached Monday-Friday 7:00 am-4:00 pm (with alternate Fridays off). If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Sharmila Landau can be reached Monday-Friday 8:00 am-5:00 pm at (571)272-0614. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

KSO

/David J Blanchard/
Primary Examiner, Art Unit 1643